


In the Claims

- 1-9 (previously cancelled)
10. (cancelled)
11. (cancelled)
12. (cancelled)
13. (previously amended) The method as claimed in claim 23, wherein said contrast agent is conjugated to a biological vector capable of targeting said contrast agent to a desired region of the body.
14. (previously amended) The method as claimed in claim 13, wherein said biological vector is selected from the group consisting of an antibody, an antibody fragment, and an oligonucleotide binding motif.
- 15-22 (previously cancelled)
23. (currently amended) A method of detecting regions with decreased vascular perfusion in a human or non-human animal subject which comprises
- a) administering to said subject an effective amount of a magnetic resonance imaging contrast agent comprising a physiologically tolerable Europium (II) ~~compound~~ chelate complex or a salt thereof wherein the chelant is selected from the group consisting of DTPA, EDTA, DTPA-BMA, DO3A, DOTA, HP-DO3A, TMT and DPDP, said ~~compound~~ chelate complex having a first

oxidation state and wherein said Europium (II) compound is oxidized *in vivo* to a Europium (III) ~~compound~~ chelate complex having a second oxidation state and said oxidation states differ in relaxivity by a factor of at least 5, whereby contrast difference is enhanced in regions with decreased vascular perfusion in which conversion between said oxidation states occurs; and
b) generating an image of said subject.



24. (cancelled)

25. (previously added) The method as claimed in claim 23, wherein said oxidation states differ in relaxivity by a factor of at least 10.

26. (previously added) The method as claimed in claim 23, wherein said oxidation states differ in relaxivity by a factor of at least 20.

27. (previously added) The method as claimed in claim 23, wherein said oxidation states differ in relaxivity by a factor of at least 100.

28. (previously added) The method as claimed in claim 23, wherein said contrast agent is conjugated to a macromolecule selected from the group consisting of proteins, polymers and liposomes.

29. (previously added) The method as claimed in claim 23, wherein said regions are tumours.

30. (previously added) The method as claimed in claim 23, wherein said regions are cardiac tissue.

31. (previously added) The method as claimed in claim 23, wherein said regions are in the brain.

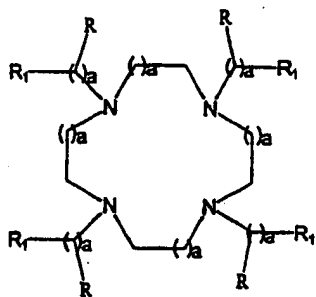
32. (previously added) The method as claimed in claim 25, wherein the method is used in the evaluation of stroke.

33. (new) A method of detecting regions with decreased vascular perfusion in a human or non-human animal subject which comprises the steps of:

(a) administering to said subject an effective amount of a magnetic resonance imaging contrast agent comprising a physiologically tolerable Europium (II) chelate complex or a salt thereof wherein the chelant is selected from the group consisting of porphyrins, phthalocyanins, crown ethers, hemin, heme, cryptands and cryptates with the proviso that the aforementioned chelants do not comprise a hydroxyaryl group at the nitrogen atoms, said Europium (II) chelate complex having a first oxidation state and being oxidized *in vivo* to a Europium (III) chelate complex having a second oxidation state and said oxidation states differ in relaxivity by a factor of at least 5, whereby contrast difference is enhanced in regions with decreased vascular perfusion in which conversion between said oxidation states occurs; and

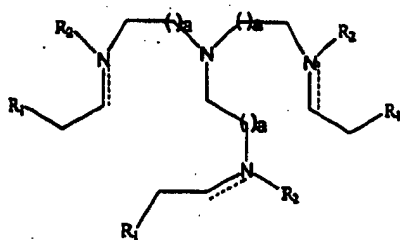
(b) generating an image of said subject.

34. (new) A method of detecting regions with decreased vascular perfusion in a human or non-human animal subject which comprises administering to said subject an effective amount of a magnetic resonance imaging contrast agent comprising a physiologically tolerable Europium (II) chelate complex or a salt thereof wherein the chelant is selected from compounds of formulae (I), (II), (III), (IV), (V) and (VI):



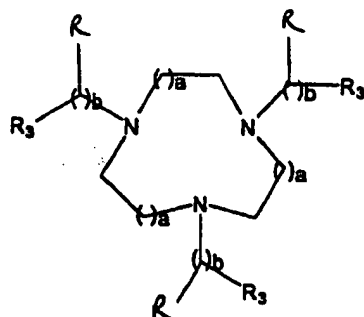
(I)

where each a independently represents an integer between 1 and 3, each R independently represents hydrogen or hydroxy and each R₁ independently represents a carboxylate, phosphate, thioacid, thiol, amino alkoxide or hydroxy group;



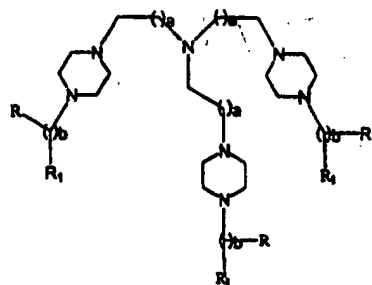
(II)

where a and R₁ are as hereinbefore defined and each R₂ independently represents hydrogen or C₁₋₆ alkyl with the proviso that R₂ is absent when the double bond is present on the same nitrogen;



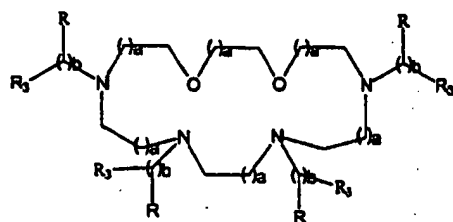
(III)

where a, R and R₂ are as hereinbefore defined, b is an integer between 0-3 and each R₃ independently represents R₁, NR-NR₂-COO⁰, or N=N-COO⁰ when b is positive or each R₃ independently represents N=CH-COO⁰ or NR₂-CH₂-COO⁰;



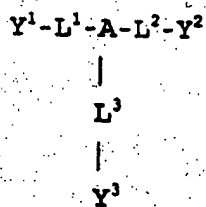
(IV)

where a, b, R and R₁ are as hereinbefore defined;



(V)

where a, b, R and R₃ are as hereinbefore defined;



(VI)



where A is N, CR₄, P, P=O, *cis,cis,cis*-1,3,5-trisubstituted-cyclohexane or an N,N',N''-trisubstituted-triaza 9 to 14 membered macrocyclic ring;

L¹, L², L³ are linker groups which are independently chosen from C₁₋₄ alkylene, C₄₋₈ cycloalkylene or C₄₋₈ o-arylene;

Y¹, Y², Y³ are independently chosen from -NH₂, -B(=O)OZ, -N=CR₅-B(=O)OZ, -NR₅-CR₆-(=O)OZ, -N[CR₆-B(=O)Q]₂ and -O-CR₆-B(=O)OZ where B is C or

PR₆, each Q is independently -OZ or -NR₆, and Z is H or a counter-ion;

each R₄ and R₅ group is independently chosen from H, C₁₋₅ alkyl, C₁₋₅ alkoxyalkyl, C₁₋₅ hydroxyalkyl, C₁₋₅ aminoalkyl, or C₁₋₆ fluoroalkyl;

R₆ is OH, C₁₋₆ alkyl, C₁₋₆ alkoxyalkyl, C₁₋₆ fluoroalkyl or C₁₋₁₀ alkoxy;

with the proviso that at least one of Y¹, Y² and Y³ is -N=CR₅-B(=O)OZ,

said Europium (II) chelate complex having a first oxidation state and being oxidized *in vivo* to a Europium (III) chelate complex having a second oxidation state and said oxidation states differ in relaxivity by a factor of at least 5, whereby contrast difference is enhanced in regions with decreased vascular perfusion in which conversion between said oxidation states occurs; and

a) generating an image of said subject.